

The Neuroscience of Resilience

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ABSTRACT

Resilience underpins human evolution and the success of the human race. Though difficult to define because of its complex nature there are fundamental neuroanatomical, neurophysiological and neurochemical pathways that are at its basic core. These pathways are expressed from our inherited genetic template but epigenesis resulting from social and environmental factors, particularly physical and mental trauma, can influence our individual resilient nature. Building resilience as we grow older has important implications for our aging society.

Keywords: Medial Prefrontal Cortex; Amygdala; Hippocampus; Epigenetics; Alzheimer's Disease

Introduction

The word resilience comes from the Latin “resilere” ... to spring back. Resilience in Homo sapiens almost certainly has genetic underpinnings. However, there are complex interactions with neurophysiological responses to the environment, coupled with underlying personality traits, which ultimately fashion a defining robust outlook [1]. The resilient individual has a positive sense of themselves and an ability to confront adversity. With resilience comes strength and the capacity to find hope and meaning in life. Without it there is inability to cope with anxiety and chronic stress which can degrade brain health over time. A loss of sense of self may result from high levels of stress hormones and dysfunction of neural connections, particularly between the amygdala, hippocampus and medial prefrontal cortex [2].

Our Identity

Some people are born resilient and early on show signs that they control matters on their own terms. However more acquire resilience than have it innately. This is usually by exposure to major stresses and being strengthened by them. They face realities with vigour, make meaning of hardship and improvise solutions finding positives in the challenges they face. They are more optimistic,

hopeful and eschew negativity. Even when under pressure resilient people keep moving forward. The American educator Yasmin Mogahed said: “Resilience means you experience, you feel, you hurt. You fall. But you keep going” [3]. Psychiatrist George Vaillant noted three human qualities that assist in people becoming more resilient: Firstly, having an orientation toward the future to enable anticipation, plans and hope. Secondly finding the capacity to love and have empathy. Finally having to seek and develop a deep connection with others with a capacity for gratitude [4]. Aristotle observed that “Happiness is the consequence of a deed”. Conceiving of and delivering such a deed is one marker of resilience (Aristotle, Nicomachean ethics).

Petrea King in her 2017 book detailed her strategies for dealing with adversity emphasising a healthy lifestyle, living a meaningful life, finding joy in the passions and pastimes of the present, and feeling valued and loved by the people with whom we share our life [5]. The wellness literature offers models and strategies for improving resilience. Biological strategies such as exercise, meditation, relaxation therapies and mindfulness in particular, can inhibit negative signals from the amygdala – the primitive threat and fear centre in our brain [6].

Our Sense of Self

Future thought is a vital component of being human and is an essential part of our sense of self. It is likely to have played a significant role in human evolution and of developing resilience. The prefrontal cortex forms a network in the brain that is involved in future planning. That network also includes the hypothalamus which is central to episodic memory formation and can track moments in sequential memory. This is vital in both imagining the future and in the orchestration of resilience [7].

A person's mind handles information about oneself differently from other details. Memories that reference the self are easier to recall than other forms of memory (the so called "self-referencing effect"). Information related to oneself is privileged and more salient in one's thoughts. Self-related thoughts are distinct from episodic memory, from specific events, and from the semantic memory of general knowledge [6].

Studies using functional MRI, highlighting blood flow and oxygen consumption, have identified the medial prefrontal cortex as the main brain region related to self-thought and its importance in the core ability to maintain our identity. The medial prefrontal cortex can be further divided into dorsal and ventral regions with each making different contributions to self-related thought. The dorsal section distinguishes self from other and appears to be task related whereas the ventral area contributes more to emotional processing. The self-referencing effect extends to both the present and future self [8].

A recent study in the *Journal of Social Cognitive and Affective Neuroscience* explores how the ventral medial prefrontal cortex (vmPFC) helps knit together memories of the present and future self. The researchers have demonstrated that lesions of the vmPFC are associated with altered personality, blunted emotions, and a number of changes in emotional and executive function [8]. There are sex differences in the behavioural inhibition system, and vmPFC connectivity, with females showing distinctly heightened sensitivity. The reasons for this difference are unclear but this may have implications for the increased incidence of severe depression and anxiety seen more recently in the female population [9].

A traumatic injury to the area of the vmPFC leads to an impaired sense of identity. These patients have little or no ability to recall references to the self, regardless of the context of time. It seems that this region may produce a fundamental model of oneself and place it in mental time. This may be the source of our sense of self and has a key role in human interactions, evaluating social context and in resilience [10].

Stress and Resilience

There are well known long term emotional and physical consequences of chronic stress. Some individuals seem to be

genetically primed to have a low threshold to experience stress from an early age precipitated by seemingly minor triggers. They may be on the autistic spectrum or have a psychiatric diagnosis of either an attention deficit or bipolar disorder [1]. More recently environmental factors, including severe physical or emotional trauma have been shown to involve epigenetic alterations to the way genes function to influence the development of chronic stress [11]. Epigenetics potentially explains why effects of trauma may endure long after the immediate threat is gone, and it is also implicated in the diverse pathways by which trauma can be transmitted to future generations [12].

There seems little doubt that chronic stress plays a major role in the resilience of individuals. Stress can cause an imbalance of neural circuitry with changes in behavioural states ranging from cognition and decision making to anxiety and mood alteration. The resulting imbalance in turn affects body physiology through neuroendocrine and metabolic mediators [1]. In the classic fight-or-flight response a threatening encounter triggers the release of stress hormones, mainly adrenaline and cortisol, which prompt a cascade of changes via the blood stream and autonomic nervous system. This is a reaction to immediate danger which should recede once the threat resolves [13].

Some individuals develop a chronic, ongoing stress disorder long after the danger has passed. This has been particularly documented in war veterans with post-traumatic stress disorder (PTSD). These individuals have a greater number of glucocorticoid receptors, proteins to which cortisol binds to exert its diverse influences [14]. Receptors for glucocorticoids are found in the hippocampus, amygdala and frontal cortex. These three brain regions are involved in memory processing and emotional regulation. MRI studies have shown that chronic exposure to stress is associated with reduced volume of both the amygdala and frontal cortex, suggesting neurotoxic effects of stress hormones on the brain [14].

Trauma, either physical or emotional, seems to reset the cortisol feedback loop which involves genetic expression of methylation. The methylation process influences RNA transcription from its DNA template in the presence of specific enzymes. In 2018 Rachel Yehuda and colleagues observed reduced methylation within the glucocorticoid receptor gene NR3C1 of veterans suffering from PTSD when compared to normal controls. The NR3C1 gene encodes and sensitises the glucocorticoid receptor which may be the explanation for recalibration of the cortisol feedback loop and altered adrenalin response in traumatised individuals [11].

High levels of stress hormones, if sustained over a long-time frame, harm the body in multiple ways especially weakening the immune and autonomic nervous systems with susceptibility to hypertension. Equally important is the searing effect on the brain with flashbacks, nightmares and irrational fears. This may lead

to ongoing mental illness and also subsequently an increased risk of dementia [15]. Stress drives inflammation and immune dysregulation in the brain impacting brain connectivity [10]. If you have fewer neural connections and synapses because of chronic stress, then dementia will appear earlier in the aging process. Studies in animals as well as human autopsy studies have linked chronic stress to a loss of neural connections in the hippocampus, the main immediate memory centre of the brain and where Alzheimer's dementia has its greatest impact [2]. Early life stress, such as childhood abuse, neglect and loss, is a well-established major risk factor for developing depressive disorders in later life. Evidence also exists for the adverse effects of early life stress on the subsequent resilience of these individuals in adulthood [12].

Resilience, Mental Illness and Dementia

Age is the biggest risk factor for dementia but there are many other influences. Genetic vulnerability is important but as well there are modifiable risk factors including smoking, hypertension, social isolation and impaired sense of vision or hearing. In our older years resilience is tested by the markers of aging and the inevitable changes that afflict the elderly [16]. In 2020 the British based Lancet Commission on dementia prevention estimated that four in 10 cases could be prevented or delayed if 12 identified and modifiable risk factors were addressed by society [17]. Certain mental conditions, particularly depression and schizophrenia, have also been linked to dementia although depression itself can also be a sign of cognitive decline [18].

Leah Richmond-Rakerd and colleagues from the University of Michigan followed 1.7million people in New Zealand over 30yrs and found that those diagnosed with a mental disorder such as anxiety, major depression or bipolar disorder had four times the rate of ultimately developing dementia. For those with a psychosis it was six times higher [15]. Some suspect that long term use of psychiatric medications could also be playing a role in the development of dementia. The evidence for this is questionable but it remains problematic. The Michigan authors do not think it is a major contributor.

People with mental illnesses may have less cognitive reserve due to a diminished number of neural connections. It is as though their "brainpower" is not robust enough to withstand normal aging without obvious loss of function [19]. This also occurs with chronic stress and trauma across generations affecting the pathways to adaptation and resilience [20]. There may be some overlap in genetic markers associated with Alzheimer's disease and those linked to bipolar disorder and major depression [19].

Conclusion

Resilience is a basic quality essential to human existence and its evolution. It has a genetic determination but is heavily influenced

by social and environmental factors. The latter can result in epigenetic changes to our DNA expression and resilient nature [12]. The neuroscientific basis for resilience is complex but likely to have been affected by the uncertain future-focused outcome of modern life. The latter has produced an increasing number of people with emotional exhaustion due to chronic time pressure and loss of work-life boundaries often contributed to by the overwhelming social media that surrounds everyone. Digitised communication and loss of human contact, particularly affirmative touch, are modern life influences in the degradation of individual resilience [21]. Other biological factors, such as lack of exercise, poor diet and inadequate sleep add to poor mental health and our ability to maintain a sense of control [1]. Uncertainty in today's society has reproduced our physiological hyper-vigilant reaction to perceived threat and is a fundamental trigger for stress and anxiety. Chronic stress, as with physical or mental trauma, can lead to neurophysiological changes in the brain influencing our evolutionary fundamental resilient nature [20-22].

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